'Normal' Controls for Intracranial MRI?

G. Darwent[1], D. A. Capener[1], I. D. Wilkinson[1], P. D. Griffiths[1], and N. Hoggard[1]
[1]MRI Unit, University of Sheffield, Sheffield, United Kingdom

Introduction
MR imaging is an extremely powerful diagnostic tool for the central nervous system. Pathology may be detected in asymptomatic individuals as the sensitivity of MRI has been shown to be equal to or better than competing technologies. (1) The bioethics surrounding the incidental findings are not straightforward and every imaging institution will encounter this situation in their control volunteers. Yet the implications for the individuals involved may be profound not only for the health of the individual but also financially, with implications for both insurance eligibility and borrowing. Should all participants have review of their imaging by an expert? If abnormalities are found, who should be informed?
We decided to review the incidental findings from two cohorts of volunteers as it was felt that abnormalities were being found in an unexpectedly high number. We chose the first 100 volunteers who underwent intracranial MR scanning on a new 3T installation (2003) and from when an existing 1.5T was previously installed (1998) in the same University research MRI Unit.

Method
The first cohort of 100 normal volunteers that were imaged on a 3T Intera MR system (Philips Medical Systems, Best, Holland) and 100 volunteers on a 1.5T Edge Eclipse (Philips Medical Systems, Best, Holland) were reviewed in this study. All participants completed a volunteer consent form in addition to a standard departmental MR safety screening form. The volunteer screening form requires the general practitioner details to be completed and asks the participant to consider closely the possibility/implications of finding an unexpected but potentially serious abnormality before signing. It also states that the participant's general practitioner and/or consultant of the appropriate speciality will be contacted.
All volunteers were then re-screened verbally before entering the magnet room in compliance with departmental protocol. A range of MR sequences was performed. No formal clinical protocols were used and protocols differed from individual to individual, however, each examination contained at least T1 or T2 weighted imaging of the whole brain. In our assessment we have not included findings that we consider of no clinical consequence in routine clinical practice such as unidentified bright objects consistent with age, so called age related changes and inflammatory mucosal disease, for example.

Results
No volunteer was asked to remain in the MR scanner for longer than one hour. General compliancy was good and no examination was terminated due to claustrophobia. The average age of the participants imaged at 3T was 38.12 years (range 21-66 years) and 29.76 years (range 21- 68 years) at 1.5T.

3T On the 3T system pathology was found in 7 volunteers. (Fig 1)

Sex	Age	Abnormality
M	23	Cavernoma
F	30	Pit lesion
F	33	?MS
F	21	Old infarct
F	46	MS
F	56	?Glioma
F	36	MS

1.5T On the 1.5T system, pathology was found in 7 volunteers. (Fig 2)

Sex	Age	Abnormality
F	66	Cerebrovascular disease
F	59	MS
F	40	Arachnoid cyst
M	36	Cerebellar atrophy
M	30	3RD ventricle colloid cyst
M	34	Corpus callosum AVM
M	23	Cavernoma

In all cases the volunteers were counselled by a senior Neuroradiologist immediately following the examination. The participant's primary care physician was informed in all cases and in one case the volunteer was referred directly to a clinical neurologist.

Discussion
On both systems unexpected pathology was found in 7% of the participants and had not changed between the first installation in 1998 and the second in 2003. No difference in the incidence of pathology was demonstrated between the different field strength scanners. It was noteworthy that our incidental pathology didn't include any cerebral aneurysms as might have been expected in a sample of this size, although the average age of these participants was relatively low. Katzman et al found a rate of 2.9% for the type of pathology that we have included here (2). Why should this be? It is clearly not safe to assume that all volunteers are normal controls as volunteers can 'self refer', having already existing symptoms. Following discussion with the volunteers after the scan, one was aware of the diagnosis of multiple sclerosis but had omitted to inform the MR Unit staff, one was aware that there had been a problem in the past but had undergone no prior investigations. No other volunteers were symptomatic.

The high incidence of abnormalities in these data raises the question of whether self referral for volunteer MRI scanning biases the control sample group. Many would advocate removal of the participant from the control group if the abnormality is deemed "relevant", which is our policy, in an attempt to avoid bias though clearly some of these abnormalities do exist in the true normal population.

Should all participants have review of their imaging by an expert? Our current practice has been agreed and developed with our local medical ethics committee and is to include whole brain T2 weighted or FLAIR weighted imaging. It is our current policy that we do have review of imaging and for abnormalities we inform and counsel the participant and inform their primary care physician. We appreciate, however, that this easy access to neuroradiology support is not the case in many research facilities and this raises the question of whether a clinical MR scan should be performed routinely on all volunteers? Sample groups may differ depending on ethnicity and lifestyle, with pathology found relevant to that group e.g. in our sample, demyelination. Should we quote the risk of finding an abnormality on the scan to volunteers before they are imaged? We do not currently do so, as in any single, individual study the exact rate will vary. It may well be an unknown at the beginning of the study and depending on sample size may never be known.

Also to be considered is the effect on the quality of life of 'normal' volunteers having been found to have unexpected pathology, e.g. in the case of the diagnosis of multiple sclerosis there may be a detrimental effect upon the individual's ability to obtain health insurance, mortgages etc.(3) Findings that turn out to be medically insignificant can still cause tremendous stress for volunteer subjects and their families (4)
If abnormalities are found who should be informed? From a purely Kantian perspective the deontological approach is to only inform the participant. However, certainly in our institution the vast majority of research is publicly funded from a combination of governmental and charitable bodies. A consequentialist response to this issue suggests that if the person involved was for example at risk of epilepsy and was a driver, the potential consequences mean that our duty to society outweighs our duty to the individual.

References
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